

**IN THE CLAIMS:**

Please cancel claims 1-20 and add claims 21-60 as follows.

1-20 (canceled)

21. A method for separating plasma components from a plasma sample containing at least albumin,  $\alpha$ -1-antitrypsin, and immunoglobulins, by electrophoresis, comprising:

(I) separating the plasma into a first and second component using a first electrophoretic separation membrane whereby the first component containing a mixture of albumin and  $\alpha$ -1-antitrypsin resides on one side of the first electrophoretic separation membrane while the second component resides on the other side of the first electrophoretic separation membrane;

(II) separating the second component into third and fourth components whereby the third component containing immunoglobulins is located on one side of a second electrophoretic separation membrane, and the fourth component resides on the other side of the second separation membrane;

(III) removing material having a molecular mass greater than immunoglobulins from the third component using a third electrophoretic separation membrane whereby immunoglobulins reside on one side of the third electrophoretic separation membrane and material having a molecular mass greater than immunoglobulins reside on the other side of the third electrophoretic separation membrane; and

(IV) separating albumin from  $\alpha$ -1-antitrypsin in the first component using a fourth separation membrane whereby  $\alpha$ -1-antitrypsin resides on one side of the fourth electrophoretic separation membrane and albumin resides on the other side of the fourth separation membrane.

22. The method according to claim 21, whereby the second component contains material having a molecular mass greater than albumin.

23. The method according to claim 21, whereby the first component migrates through the first electrophoretic separation membrane.

24. The method according to claim 21, whereby the fourth component contains material having a molecular mass less than immunoglobulins contained in the third component.

25. The method according to claim 21, whereby  $\alpha$ -1-antitrypsin migrates through the fourth electrophoretic separation membrane.

26. The method according to claim 21, whereby step (I) further comprises:

(a) placing the plasma in a first solvent stream, the first solvent stream being separated from a second solvent stream by the first electrophoretic separation membrane having a molecular mass cut-off more than the molecular mass of albumin, and the second solvent stream being further bounded by a restriction membrane having a molecular mass cut off less than the first electrophoretic separation membrane;

(b) selecting a buffer for the first solvent stream having a pH greater than the pI of albumin;

- (c) applying an electric potential between the two solvent streams whereby albumin and  $\alpha$ -1-antitrypsin migrate through the first electrophoretic membrane into the second solvent stream while material having a molecular mass greater than albumin and  $\alpha$ -1-antitrypsin are substantially prevented from passing through the first electrophoretic membrane;
- (d) optionally, periodically stopping and reversing the electric potential whereby material having a molecular mass greater than albumin and  $\alpha$ -1-antitrypsin that have entered the first electrophoretic membrane move back into the first solvent stream, while substantially preventing albumin or  $\alpha$ -1-antitrypsin in the second solvent stream from re-entering the first solvent stream;  
and
- (e) maintaining steps (c) and optionally (d) until the desired amount of albumin and  $\alpha$ -1-antitrypsin migrates into the second solvent stream;

27. The method according to claim 26, whereby the material having a molecular mass less than albumin and  $\alpha$ -1-antitrypsin move through the first separation membrane and the restriction membrane.

28. The method according to claim 21, whereby step (II) further comprises:

- (f) placing the second component in a third solvent stream, the third solvent stream being separated from a fourth solvent stream by a second electrophoretic separation membrane having a molecular mass cut-off less than the molecular mass of immunoglobulins;
- (g) selecting a buffer for the third solvent stream having a pH above neutral;
- (h) applying an electric potential between the third and fourth solvent streams whereby immunoglobulins from the second component are substantially prevented from passing through the second electrophoretic separation membrane thereby forming the third component while material having a molecular mass less than that of immunoglobulins in the second component migrate through the second electrophoretic separation membrane into the fourth solvent stream to form the fourth component;
- (i) optionally, periodically stopping and reversing the electric potential whereby materials from the third component that have entered the second electrophoretic separation membrane move back into the third solvent stream while preventing materials from the fourth component from re-entering the third solvent stream; and
- (j) maintaining steps (h) and optional (i) until the desired amount of third component has been separated from the fourth component;

29. The method according to claim 28 whereby step (III) further comprises:

- (l) replacing the second electrophoretic separation membrane with a third electrophoretic separation membrane having a molecular mass cut-off greater than the molecular mass of immunoglobulins;
- (m) selecting a buffer for the third solvent stream having a pH below neutral;
- (n) replacing the fourth solvent stream with a fresh fourth solvent stream;
- (o) applying an electric potential between the third solvent stream and the fresh fourth solvent stream whereby immunoglobulins in the third component migrate through the third electrophoretic separation membrane into the fresh fourth solvent stream;
- (p) optionally, periodically stopping and reversing the electric potential whereby material having a molecular mass greater than immunoglobulins in the third component that have entered

the third electrophoretic membrane move back into the third solvent stream while preventing immunoglobulins in the fresh fourth solvent stream from re-entering the third solvent stream; and (q) maintaining steps (o) and optional (p) until the desired amount of immunoglobulins migrate to the fresh fourth solvent stream.

30. The method according to claim 21, whereby step (IV) further comprises:

(r) placing the first component in a fifth solvent stream, the fifth solvent stream being separated from a sixth solvent stream by a fourth electrophoretic separation membrane having a molecular mass cut-off less than the molecular mass of albumin;

(s) selecting a buffer for the fifth solvent stream having a pH greater than neutral;

(t) applying an electric potential between the fifth and sixth solvent streams whereby  $\alpha$ -1-antitrypsin migrates through the fourth electrophoretic separation membrane into the sixth solvent stream while albumin is substantially prevented from passing through the fourth electrophoretic separation membrane;

(u) optionally, periodically stopping and reversing the electric potential whereby albumin that has entered the fourth electrophoretic separation membrane moves back into the fifth solvent stream while preventing  $\alpha$ -1-antitrypsin in the sixth solvent stream from re-entering the fifth solvent stream; and

(v) maintaining steps (t) and optionally (u) until the desired amounts of albumin and  $\alpha$ -1-antitrypsin are separated on opposite sides of the fourth separation membrane.

31. The method according to claim 21, further comprising using more than one electrophoretic separation apparatus.

32. The method according to claim 21, further comprising using three electrophoretic separation apparatus.

33. The method according to claim 6 whereby the first electrophoretic separation membrane of step (a) has molecular mass cut-off of about 75 kDa and the restriction membrane has a molecular mass cut off of about 50 kDa.

34. The method according to claim 26 whereby the first electrophoretic separation membrane of step (a) has a molecular mass cut-off greater than 67 kDa.

35. The method according to claim 26 whereby the buffer in step (b) has a pH of about 9.

36. The method according to claim 26 whereby the buffer is a Tris-borate buffer.

37. The method according to claim 26 whereby the electric potential applied in step (c) is 250 volts.

38. The method according to claim 28 whereby the second electrophoretic separation membrane of step (f) has a molecular mass cut-off of about 200 kDa.

39. The method according to claim 28 whereby the second electrophoretic separation

membrane of step (f) has a molecular mass cut-off greater than 150 kDa.

40. The method according to claim 28 whereby the buffer of the third solvent stream in step (g) has a pH of about 9.

41. The method according to claim 28 whereby the electric potential applied in step (h) is 250 volts.

42. The method according to claim 29 whereby the third electrophoretic separation membrane of step (l) has a molecular mass cut-off of about 500 kDa.

43. The method according to claim 29 whereby the buffer of the immunoglobulins concentrate of step (m) has a pH of less than 5.

44. The method according to claim 29 whereby buffer has a pH of about 4.6.

45. The method according to claim 29 whereby the electric potential applied in step (o) is 250 volts.

46. The method according to claim 30 whereby the fourth electrophoretic separation membrane of step (q) has molecular mass cut-off of about 50 kDa.

47. The method according to claim 30 whereby the fourth electrophoretic separation membrane of step (q) has molecular mass cut-off less than 54 kDa.

48. The method according to claim 30 whereby the buffer of the fifth solvent stream in step (r) has a pH of about 8.0.

49. The method according to claim 30 whereby the buffer is a Tris-borate buffer.

50. The method according to claim 30 whereby the electric potential applied in step (t) is 250 volts.

51. The method according to any one of claims 21-50, whereby albumin, immunoglobulin, and  $\alpha$ -1-antitrypsin are separated from plasma.

52. The method according to any one of claims 21-50 whereby the immunoglobulins are immunoglobulin G (IgG).

53. The method according to any one of claims 21-50 whereby yields of albumin, immunoglobulins and  $\alpha$ -1-antitrypsin from plasma are at least 70% and purity of at least 90%.

54. The method according to any one of claims 21-50 whereby albumin, immunoglobulins and  $\alpha$ -1-antitrypsin are separated from plasma in less than 1 day.

55. The method according to any one of claims 21-50 whereby albumin, immunoglobulins and  $\alpha$ -1-antitrypsin are separated from plasma in less than 12 hours.

56. The method according to any one of claims 21-50 whereby albumin, immunoglobulins and  $\alpha$ -1-antitrypsin are separated from plasma in less than 6 hours.

57. The method according to any one of claims 21-50 whereby the plasma is a pooled human plasma sample.

58. The method according to claim 21, 26 or 30 whereby step (IV) is carried out after step (I).

59. A method for separating plasma components from a plasma sample by electrophoresis, comprising:

(I) separating the plasma into a first and second component in a first electrophoretic separation apparatus using a first electrophoretic separation membrane having a molecular mass cut-off of about 200 kDa, whereby the first component containing a mixture of albumin and  $\alpha$ -1-antitrypsin resides on one side of the first electrophoretic separation membrane while the second component resides on the other side of the first electrophoretic separation membrane;

(II) removing undesired material from the first component in a second electrophoretic separation apparatus using a second electrophoretic separation membrane having a molecular mass cut-off of about 80 kDa, whereby albumin and  $\alpha$ -1-antitrypsin reside on one side of the second electrophoretic separation membrane and the undesired material resides on the other side of the third electrophoretic separation membrane;

(III) separating albumin from  $\alpha$ -1-antitrypsin in the first component using a third separation membrane having a molecular mass cut-off of about 40 kDa in a third electrophoretic separation apparatus, whereby  $\alpha$ -1-antitrypsin resides on one side of the third electrophoretic separation membrane and albumin resides on the other side of the third separation membrane; and

(IV) separating the second component into third and fourth components whereby the third component containing immunoglobulins is located on one side of a fourth electrophoretic separation membrane, and the fourth component resides on the other side of the fourth separation membrane.

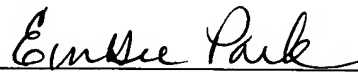
60. The method according to claim 59, whereby the first, second, and third electrophoretic separation apparatus are connected together in steps (I) – (III), and the first electrophoretic separation is disconnected from the second or third electrophoretic separation apparatus in step (IV).

No fee is believed due with the filing of this preliminary amendment. If any fee is due, however, the Commissioner is hereby authorized to charge payment to Deposit Account No. 02-0393. If any additional fees associated with this communication are required or to credit any overpayment, please use Deposit Account No. 02-0393.

If a telephone interview would be of assistance in advancing prosecution of the subject application, the Examiner is requested to telephone the undersigned at the number provided below.

Dated: August 1, 2003

Respectfully submitted,



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## **STATEMENT OF STATUS AND SUPPORT FOR CLAIM CHANGES**

The claims 1-20 are pending in the application. Please cancel claims 1-20.

New claims 21-60 are being added in this reissue application.

Claim 21 recites a method of separating albumin,  $\alpha$ -1-antitrypsin, and immunoglobulins by electrophoresis. This method is described generally in Column 4, lines 27-37, and in great detail in Column 7, line 13 to Column 8, line 5 and Column 10, line 38 to Column 11, line 19. For example, step (I), separating the plasma into a first and second component using a first electrophoretic separation membrane, is described at Column 7, lines 15-25 and Column 10, lines 50-65. Step (II), separating a third component containing immunoglobulins from a fourth component, is described at Column 7, lines 40-44 and Column 11, 6-13. Step (III), removing material having a molecular mass greater than immunoglobulins from the third component, is described in Column 7, lines 44-49. Step (IV), separating albumin from  $\alpha$ -1-antitrypsin, is described in Column 7, line 65 to Column 8, line 3 and Column 10, line 65 to Column 11, line 6.

Claim 22 is described in Column 7, lines 15-25.

Claim 23 is described in Column 7, lines 15-25.

Claim 24 is described in Column 7, lines 36-44.

Claim 25 is described in Column 7, lines 44-49.

Claim 26 is described in Column 2, lines 27-62 and Column 12, lines 15-53.

Claim 27 is described in Column 7, lines 15-25.

Claim 28 is described in Column 2, lines 64 to Column 3, line 30 and Column 12, line 53 to Column 13, line 19.

Claim 29 is described in Column 3, lines 34-63 and Column 13, lines 20-58.

Claim 30 is described in Column 3, lines 65 to Column 4, line 26 and Column 13, line 59 to Column 14, line 15.

Claim 31 is described in Column 5, lines 4-12, Column 10, line 38 to Column 11, line 6.

Claim 32 is described in Column 10, line 38 to Column 11, line 6.

Claim 33 is described in Column 4, lines 41-43 and Column 14, lines 20-24.

Claim 34 is described in Column 1, lines 36-37 and Column 4, lines 41-43.

Claim 35 is described in Column 4, lines 46-47 and Column 14, lines 24-25.

Claim 36 is described in Column 4, lines 47-49 and Column 14, lines 26-27.

Claim 37 is described in Column 4, line 65 to Column 5, line 3 and Column 14, lines 48-49.

Claim 38 is described in Column 4, lines 50-53 and Column 14, lines 28-30.

Claim 39 is described in Column 1, lines 50-53 and Column 4, lines 50-53.

Claim 40 is described in Column 4, lines 55-56 and Column 14, lines 34-35.

Claim 41 is described in Column 4, line 65 to Column 5, line 3 and Column 14, lines 48-49.

Claim 42 is described in Column 4, lines 52-54 and Column 14, lines 31-33.

Claim 43 is described in Column 4, lines 56-57 and Column 14, lines 36-38.

Claim 44 is described in Column 4, lines 56-58 and Column 14, lines 39-40.

Claim 45 is described in Column 4, line 65 to Column 5, line 3 and Column 14, lines 48-49.

Claim 46 is described in Column 4, lines 59-60 and Column 14, lines 41-43.

Claim 47 is described in Column 1, lines 55-57 and Column 4, lines 59-60.

Claim 48 is described in Column 4, line 61 and Column 14, lines 44-45.

Claim 49 is described in Column 4, lines 61-63 and Column 14, lines 46-47.

Claim 50 is described in Column 4, line 65 to Column 5, line 3 and Column 14, lines 48-49.

Claim 51 is described in Column 2, line 25 to Column 5, line 3; and Column 5, lines 18 – 40; Column 7, line 12 to Column 8, line 5; column 10, lines 38 to Column 11, line 35.

Claim 52 is described in Column 4, lines 38-39; Column 5, lines 33-34; Column 7, lines 35-49; Column 9, lines 37-63; Column 11, lines 7-19; and Column 14, lines 50-51.

Claim 53 is described in Column 5, lines 18-20; Column 9, lines 13-16; Column 9, 54-56; Column 9, lines 65-66; Figure 6; column 11, lines 14-16 and Column 14, lines 52-53.

Claim 54 is described in Column 5, lines 22-24 and Column 11, lines 14-19 and Column 14, lines 55-57.

Claim 55 is described in Column 5, lines 22-24; Column 11, lines 14-19 and Column 14, lines 58-60.



Claim 56 is described in Column 5, lines 22-25; Column 11, lines 14-19 and Column 14, lines 61-63.

Claim 57 is described in Column 4, lines 35-37; and Column 7, line 13 to Column 8, line 5; .

Claim 58 is described in Column 4, lines 27-29, and Column 14, lines 16-17.

Claim 59 is described in Column 10, lines 50-67 to Column 11, lines 1-6.

Claim 60 is described in Column 11, lines 7-13.